Preface

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The 42nd Annual Symposium on the Biology of Skin addressed "The Genetics of Skin Disease" in Snowmass Village, Colorado from July 24 to 28, 1993. This year's meeting presented the opportunity to discuss how modern approaches to molecular genetics and molecular biology have been applied to understanding the mechanisms of skin disease. It also allowed us to explore the potential for using approaches in gene therapy to correct genetic defects in structural proteins. The meeting brought together biochemists; molecular, cellular, and developmental biologists; ultrastructural biologists; pharmacologists; molecular geneticists; cutaneous biologists; and academic and clinical dermatologists, geneticists, and pediatricians. Scientists from academic departments, research institutes, biotechnology companies, and the pharmaceutical industry were all well represented. Twenty three speakers and sixteen poster presenters participated in the meeting.

By design, the Symposium on the Biology of Skin has brought together cutaneous biologists with other scientists in basic and clinical research fields to consider in detail one aspect of cutaneous biology. These meetings have served as a forum where established and developing scientists, as well as students and trainees, could all meet to discuss a single topic in detail, bringing to bear their different perspectives on the problem at hand. These meetings and their published proceedings have shown how the skin can be a model for the study of universal mechanisms in biology. By combining the approaches of scientists outside of the normal sphere of cutaneous biology with those accustomed to using the skin as a means to study biology, this symposium has often produced fresh perspectives and launched new research adventures.

It is an opportune time to examine "The Genetics of Skin Disease." By a combination of fortune and concerted effort in government, funding for basic research in the structural disorders of the skin such as epidermolysis bullosa has directed application of modern techniques in molecular genetics to the study of these diseases. The first part of this meeting considered diseases involving genetic defects in structural proteins of the epidermis and dermis. Pioneering ultrastructural studies that helped to define the location of the abnormal proteins in the disorders of keratinization and in epidermolysis bullosa were proved correct by elegant studies that localized molecular defects in simplex, junctional, dominant dystrophic, and recessive dystrophic epidermolysis bullosa and in epidermolytic hyperkeratosis. Elegant research has also defined genetic mutations in Ehlers-Danlos syndromes, Marfan syndrome, and pseudoxanthoma elasticum.

The identification of the precise mutations and the altered proteins that characterize this group of diseases of the dermis and epidermis raise the intriguing possibility that gene therapy approaches may be applied to reverse the phenotype of these diseases. These possibilities were discussed thoroughly, considering especially the facility of using transfected keratinocytes as a means of delivering the transgenes. In addition, modern techniques such as homologous recombination and the use of anti-sense approaches or ribozymes to inhibit transcription and expression of the products of mutated genes were discussed. We are on the threshold of gene therapy trials to correct the central genetic defects in several forms of epidermolysis bullosa.

The topic of the Symposium shifted from structural protein mutations to malignant transformation. The interaction of genetic determinants of ultraviolet light sensitivity and mutations in a limited number of oncogenes and tumor suppressor genes is associated with the development of melanoma and non-melanoma skin cancers. These diseases are important medical problems and also provide important models for the study of multistage carcinogenesis and UV-induced transformation. Identification of the susceptibility genes for melanoma and nevoid basal cell carcinoma syndrome will help us understand the induction of cancer; modulation of mutated genes in these tumors may allow us to alter their aggressiveness.

The genetics of other complex processes in the skin are also being better understood through application of techniques of modern genetics. The genetics of pigmentation has moved in a particularly rapid fashion in the past five years as the genetic bases for mouse and human models of dyspigmentation have been characterized. Autoimmune diseases involving the skin are complex polygenic processes whose genetic character is now being appreciated. Finally psoriasis, one of the most common and fascinating skin diseases, is also being approached genetically, with great promise for identifying the genetic loci that determine the psoriatic phenotype.

The organizers of the Symposium on the Biology of Skin have designed a meeting true to the principles established by Dr. William Montagna and continued by Dr. Kirk Wuepper. The Symposium continues to be a crucible for the amalgamation of different approaches and ideas and for creating better understanding of basic biologic processes in the skin. This supplement in *The Journal of Investigative Dermatology* allows us to extend the influence of this gathering to the journal subscribers who encompass the corpus of cutaneous biology.

We wish to thank Ms. Beverly Polt and Ms. Cheryl Burns who organized the meeting and the affairs of Cutaneous Biology Foundation during the year. We also appreciate the support of the officers and Directors of the Cutaneous Biology Foundation who oversee the planning and financial support of the meeting. This conference has been supported for the past 27 years by a conference grant from the National Institutes of Health, and has also been faithfully supported by a number of firms in the pharmaceutical and cosmetics industry. We also wish to thank the Editor of the *JID*, Dr. Edward O'Keefe, for his support for publication of the proceedings and for preparing the manuscripts for publication.

These proceedings demonstrate clearly how modern approaches in genetics have allowed us to better understand the mechanism of a variety of important skin diseases, from mechanobullous disorders to malignancy to autoimmunity and inflammatory dermatoses. These diseases may be life-threatening, incapacitating, or merely a major impediment to a comfortable life. Their incidence ranges from the common to the rare. Not only will we be able to better understand their mechanisms and design better treatments for their control, but we may even reverse their basic nature by the application of evolving gene therapy techniques.

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